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(57) Abstract

An active agent intermediate for a noncorrosive antimicrobial composition includes between 0.25 to 2.0 % available iodine from an iodophor including a carrier acting as a solubilizing agent for said iodine; and 20.0 to 50.0 % short chain fatty acid(s). A substantially noncorrosive antimicrobial composition includes between 0.25 to 2.0 % available iodine from an iodophor, 20.0 to 50.0 % short chain fatty acid(s) and 15.0 to 45.0 % buffer. Methods for preparing the intermediate and composition and methods for using the composition are also disclosed.

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# ANTIMICROBIAL COMPOSITION AND METHOD OF PREPARATION

## Technical Field

The present invention relates generally to the sanitizer, disinfectant and antiseptic field.

## Background of the Invention

Compositions with antimicrobial properties have long been known in the art. Known antimicrobial agents include: (1) acids, such as, acetic, benzoic, boric, hydrochloric, nitric, phosphoric, sulfuric; (2) alkalis, such as calcium hydroxide, sodium hydroxide, potassium hydroxide, trisodium phosphate, sodium borate, sodium carbonate; (3) aldehydes, such as, acetyl aldehyde, formaldehyde, glyceraldehyde; (4) aromatic oils, such as camphor, cinnamon, peppermint, pine; (5) dyes, such as acridine and malachite green; (6) sulfonamides, such as sulfanilamide, sulfathiazole, sulfapyridine. Additional known antimicrobial agents include: (7) alcohols, such as methyl, ethyl, isopropyl, benzyl; (8) coal-tar derivatives, such as, phenol, para-nitrophenol; (9) reducing agents, such as carbon monoxide, sodium thiosulfate; (10) oxidizing agents, such as, bromine, chorine, iodine, perochloric

acid, sodium permanganate; (11) surface active agents, such as anionics (sulfonates), cationics (quaternary ammonium salts), non-ionics (alkylated aryl polyether alcohol); and (12) metal salts of, for example, aluminum, cobalt, copper, iron, mercury, silver and zinc.

These and other antimicrobial agents are used in one form or another in hospitals, eating and drinking establishments, dairies, food processing plants and homes among other places to kill various microorganisms including bacteria, fungi, viruses and protozoans. Particularly, these antimicrobial agents are referred to as disinfectants when applied to inanimate objects to kill microorganisms and antiseptics when applied to living tissue to kill microorganisms.

An ideal antimicrobial agent or composition would rapidly destroy bacteria, fungi, viruses and protozoans, not be corrosive and not destroy or discolor materials on which it is utilized and not be rapidly inactivated by organic matter. Despite advances made through the years in the development of antimicrobial agents and compositions, an ideal agent or composition that would maintain its efficacy in an organic matter environment and destroy all of these organisms without causing any residual toxic side effects is yet to be developed. Accordingly, a need exists for an improved antimicrobial composition more closely meeting the desirable characteristics and properties described.

Summary of the Invention

Accordingly, it is a primary object of the present invention to provide an improved antimicrobial

composition that is relatively easy and inexpensive to produce.

Another object of the present invention is to provide a safe (noncaustic or noncorrosive to both animate and inanimate objects) and effective (retainings it germicidal activity over a wide range of environmental conditions) germicide.

Yet another object of this invention is to provide a novel composition providing enhanced antimicrobial activity so as to be effective against bacteria, fungi, viruses and protozoans. Additionally, residual toxic side effects are minimized.

Other objects and advantages of the invention will become apparent as the description thereof proceeds. In satisfaction of the foregoing objects and advantages, there is provided by this invention an improved active agent intermediate for the preparation of a substantially non-corrosive antimicrobial composition. The active agent intermediate comprises by weight percent 0.25 to 2.0% iodine in an iodophor including a carrier acting as a solubilizing agent for the iodine. Iodophors, of the type described are well-known in the art. Such iodophors typically exhibit enhanced bactericidal activity of iodine, reduced vapor pressures and reduced odor. Additionally, iodophors do not tend to stain and, advantageously, wide dilution with water is possible so that various concentrations of iodophor may be utilized.

The active agent intermediate also includes from 20.0 to 50.0% short chain fatty acid(s) selected from a group consisting of formic acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, isovaleric acid, lactic acid, and mixtures thereof.

In accordance with a further aspect of the present invention, a substantially non-corrosive antimicrobial composition providing significantly enhanced antimicrobial activity is provided. The composition includes an active agent intermediate of the type described comprising a mixture of iodophor and short chain fatty acid(s). As is known in the art, the iodophor includes iodine and a carrier acting as a solubilizing agent for the iodine. Preferably, that carrier is a non-ionic surfactant such as, for example, nonoxynol or Monosan-IOD. This composition is then buffered to a pH of between 3.5 to 4.5 and preferably 3.9 utilizing any of a number of buffering agents known to those skilled in the art. Such buffering agents include any inorganic and organic bases and salts known to be useful as buffers.

As described in greater detail below, the resulting substantially non-corrosive antimicrobial composition takes advantage of the best antimicrobial properties of iodophors and short chain fatty acids. The unique chemistry of the composition prevents inactivation of the active agent by environmental contaminants and particularly those of organic origin. Further, the iodophor and short chain fatty acid(s) function together to provide a synergistic beneficial effect resulting from an interaction of these materials that is described in greater detail below.

In accordance with still another aspect of the present invention, methods are provided for the preparation of the active agent intermediate and the antimicrobial compositions described. Further, methods are provided for utilization of the compositions as antiseptics and disinfectants.

Detailed Description of the Invention

As indicated above, the present invention is drawn to novel active agent intermediates for the preparation of substantially non-corrosive antimicrobial compositions as well as those compositions. Advantageously, the compositions combine the antimicrobial activity of iodine and short chain fatty acid(s) to obtain an enhanced microbicidal synergistic effect.

Specifically, the compositions have a resulting unique chemistry that substantially prevents inactivation of the active antimicrobial agents by environmental contaminants and particularly organic environmental contaminants. Through buffering, the composition is also made effectively non-corrosive. Further, the antimicrobial activity is effective against a wide range of microorganisms and is exhibited over a wide range of environmental conditions. Accordingly, the compositions have a wide range of industrial and institutional applications including utilization as a sanitizer, disinfectant and antiseptic. The unique chemistry and synergistic effect obtained is described in greater detail in the following discussion.

In accordance with the present method, an active agent intermediate for the preparation of substantially noncorrosive antimicrobial compositions includes by weight percent substantially 0.25 - 2.0% free iodine as an iodophor and substantially 20.0 - 50.0% short chain fatty acid(s). As is well known in the art, an iodophor includes surface active agents such as non-ionic surfactants, that act as carriers for solubilizing iodine. Iodine is a potent oxidizing agent that is known in the art to bring about

irreversible damage to biological membranes of various microbial life forms. For example, iodine is known to oxidize tyrosine amino acid residues. Accordingly, iodine is known to effectively cause irreversible damage through oxidation of membrane proteins of various microbial life forms and thereby provide the desired antimicrobial action.

Many iodophor compositions are known in the art and commercially available. Such iodophors, utilizing nonoxynol-like compounds as carriers to provide a source of iodine include Bardyne I-20, Biopal CBL-10, Dermavine, Idonyx, Iobac, Ioprep, Iosan, Kleenodyne, Providine-Iodine, Rhudane, Showersan, Wescodyne and Westamine X.

Short chain fatty acid(s) including, for example, formic acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, isovaleric acid, lactic acid and mixtures thereof are known to have antimicrobial properties due to their ability to also interact with biological membranes.

While it should be appreciated that the antimicrobial activity of both iodine and short chain fatty acid(s) is known, the present invention is believed to be the first time that these two components have been combined either in an active agent intermediate for the preparation of an antimicrobial composition or an antimicrobial composition. Further, this novel combination has led to a surprising and completely unpredictable synergistic antimicrobial activity. In particular, as shown and demonstrated in detail in the examples that follow, the intermediates and compositions of the present invention exhibit significantly enhanced antimicrobial activity against an extremely wide range of organisms including

bacteria, fungi, viruses and protozoans. Further, this activity remains uncompromised in the presence of organic matter routinely found in the environment. No existing intermediate or antimicrobial composition known to the inventors exhibits anything approaching this uncompromised, broad-spectrum germicidal activity. As a result, the intermediates and compositions of the present invention have far reaching applications and may in fact be utilized as a substitute for a number of different disinfectants, antiseptics, germicides or sanitizers of more organism specific destructive nature as are presently available in the marketplace.

The reason for the unique, powerful and wide ranging antimicrobial activity resulting from this novel combination is not yet fully understood. It is theorized, however, that the short chain fatty acid(s) and iodine react to form complexes with a formula R-COOH:I. Alternatively, iodized short chain fatty acid mixtures of indefinite composition are formed. In any event, the enhanced, wide ranging antimicrobial activity is real. The synergistic microbicidal activity, resulting in an enhanced degree and scope of action, is hypothesized to be due to enhanced interaction of the components with the biological membranes thereby causing rapid and irreversible damage.

The substantially noncorrosive antimicrobial compositions prepared in accordance with the present method comprise by weight percent: substantially 0.25 - 2.0% available iodine presented as an iodophor including a carrier acting as a solubilizing agent for the iodine; substantially 20.0 - 50.0% short chain fatty acid(s) (i.e. formic acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid,

isovaleric acid, lactic acid, and mixtures thereof) and 15.0 - 45.0% buffering agent. The buffering agent is necessary to render the iodophor-short chain fatty acid active agent intermediate substantially noncorrosive and therefore environmentally safe. In order to maintain the desirable antimicrobial activity, it is necessary to buffer the iodophor-short chain fatty acid intermediate to a pH value similar to the disassociation constants of the short chain fatty acid(s) utilized in the composition. Accordingly, buffering is utilized to preferably bring the compositions to a pH of between 3.5 and 4.5. For example, a pH of approximately 3.9 is provided when utilizing a mixture of propionic and lactic acids.

As known in the art, any inorganic and organic bases and salts may be utilized for buffering. Specific examples of various buffering agents are found throughout the literature. A representative list, presented as an example and not to be limited thereto includes: alanine, ammonia, ammonium acetate, ammonium benzoate, ammonium bicarbonate, ammonium hydroxide, benzoic acid, beryllium hydroxide, calcium acetate, calcium carbonate, calcium hydroxide, calcium tartrate, deuteroammonium hydroxide, diethylamine, glutamic acid, hydrazine, hydroxylamine, magnesium acetate, magnesium benzoate, manganese carbonate, manganese sulfate, potassium acetate, potassium bicarbonate, potassium carbonate, potassium citrate, potassium hydroxide, potassium phosphate, quinine, quinoline, sodium acetate, sodium ascorbate, sodium bicarbonate, sodium bisulfate, sodium carbonate, sodium citrate, sodium hydroxide, sodium phosphate, silver hydroxide and zinc hydroxide.

As specifically shown in the following

examples, the active agent intermediate is prepared by mixing by weight percent substantially 0.25 to 2.0% available iodine from an iodophor with 20.0 to 50.0% short chain fatty acid(s) in a mixing vessel. The mixing may be completed at approximately 25°C. The intermediate may next be diluted with water to bring it to the desired concentration or activity for any particular application. Alternatively, dilution with water may be made after preparation of the composition by addition of buffering agent as described below. Specifically, the composition may be diluted to between 50-800 parts water to 1 part iodophor and short chain fatty acid(s). Based upon the type of application as pertaining to specific disinfection, the effective range of iodine in the resulting composition may be adjusted from between 0.25% (w/v) up to 2% (w/v). Again, based on the type of application, the effective range of short chain fatty acid(s) may be adjusted from 20-50% (w/v).

The antimicrobial compositions may then be prepared by adding the appropriate amount of buffering agent. When preparing the composition, it should also be appreciated that the addition of the buffering agent may result in a loss of some homogeneity, due to iodophor precipitation, and, accordingly, bactericidal efficacy, due to loss of free iodine. Thus, it is necessary to ensure sufficient carrier such as a non-ionic surfactant is present. The amount of carrier used is based on the amount of free iodine and the pH of the composition. Specifically, the amount of carrier in the composition may be adjusted based upon the amount of free iodine present and the type and amount of short chain fatty acid(s) utilized to between 6.0 and 25.0% by weight. The higher the concentration

of free iodine and the higher the pH, the more carrier required.

The following examples are to further illustrate the invention but it is not to be considered as limited thereto.

**********

Example 1

In a stainless steel mixing vessel, 0.83 ml of an iodophor, Bardyne I-20 (providing 20% titratable iodine, 1.25% (w/v)), is carefully blended by constant stirring into a mixture of 10.0 ml of propionic acid and 10.2 gm of lactic acid at 25°C until dissolved. The resulting active agent intermediate is then buffered and stabilized utilizing 15.5 ml of Product No. 92 buffering and stabilizing composition available from Valar International, LTD. of Versailles, Kentucky. Specifically, the buffering and stabilizing agent is blended slowly to homogeneity by constant stirring at 25°C and 65.3 ml of water is added while stirring continues to obtain a buffered stabilized homogenate. The resulting formulation after mixing all the ingredients has an effective pH between 3.8 and 4.0 and 0.25% available iodine.

Example 2

In a glass lined mixing vessel, 1.7 ml of iodophor (Bardyne I-20 providing 20% titratable iodine, 2.5% (w/v)), is carefully blended by constant stirring into a mixture of 10.0 ml of propionic acid and 10.2 gm of lactic acid at 25°C until dissolved. The resulting active agent intermediate is then stabilized and buffered by adding 17.0 ml of Product No. 92 buffering and stabilizing composition and blending slowly to

homogeneity by constant stirring at 25°C. 62.9 ml of water is then added while stirring continues to obtain a buffered, stabilized homogenate. The resulting composition has an effective pH of between 3.8 and 4.0 and 0.5% available iodine.

Example 3

In a glass lined mixing vessel, 3.3 ml of iodophor (Bardyne I-20 providing 20% titratable iodine, 5.0% (w/v)), is carefully blended by constant stirring into mixture of 10.0 ml of propionic acid and 10.2 gm of lactic acid at 25°C until dissolved. The resulting active agent intermediate is then stabilized and buffered by adding 17.0 ml of Product No. 92 buffering and stabilizing composition and blending slowly to homogeneity by constant stirring at 25°C. 61.2 ml of water is then added while stirring continues to obtain a buffered, stabilized homogenate. The resulting composition has an effective pH of between 3.8 and 4.0 and 1.0% available iodine.

Example 4

In a glass lined mixing vessel, 6.6 ml of iodophor (Bardyne I-20 providing 20% titratable iodine, 10% (w/v)), is carefully blended by constant stirring into mixture of 10.0 ml of propionic acid and 10.2 gm of lactic acid at 25°C until dissolved. The resulting active agent intermediate is then stabilized and buffered by adding 18.0 ml of Product No. 92 buffering and stabilizing composition and blending slowly to homogeneity by constant stirring at 25°C. 56.9 ml of water is then added while stirring continues to obtain a buffered, stabilized homogenate. The resulting

composition has an effective pH of between 3.8 and 4.0 and 2.0% available iodine.

Example 5

In a glass lined mixing vessel, 0.83 ml of iodophor (Bardyne I-20 providing 20% titratable iodine, 1.25% (w/v)), is carefully blended by constant stirring into a mixture of 20.0 ml of propionic acid and 20.3 gm of lactic acid at 25°C until dissolved. The resulting active agent intermediate is then stabilized and buffered by adding 35.0 ml of Product No. 92 buffering and stabilizing composition and blending slowly to homogeneity by constant stirring at 25°C. 27.5 ml of water is then added while stirring continues to obtain a buffered, stabilized homogenate. The resulting composition has an effective pH of between 3.8 and 4.0 and 0.25% available iodine.

Example 6

In a glass lined mixing vessel, 1.7 ml of iodophor (Bardyne I-20 providing 20% titratable iodine, 2.5% (w/v)), is carefully blended by constant stirring into mixture of 20.0 ml of acetic acid and 20.0 ml of formic acid (88% assay). The resulting active agent intermediate is then stabilized and buffered by adding 40 ml of Product No. 92 buffering and stabilizing composition and blending slowly to homogeneity by constant stirring at 25°C. 18.3 ml of water is then added while stirring continues to obtain a buffered, stabilized homogenate. The resulting composition has an effective pH of between 3.8 and 4.0 and 0.5% available iodine.

Example 7

In a glass lined mixing vessel, 0.83 ml of iodophor (Bardyne I-20 providing 20% titratable iodine, 1.25% (w/v)), is carefully blended by constant stirring into mixture of 10.0 ml of propionic acid and 10.0 ml of formic acid (88% assay) at 25°C. The resulting active agent intermediate is then stabilized and buffered by adding 8 ml of Product No. 92 buffering and stabilizing composition and blending slowly to homogeneity by constant stirring at 25°C. 72.17 ml of water is then added while stirring continues to obtain a buffered, stabilized homogenate. The resulting composition has an effective pH of between 3.8 and 4.0 and 1.0% available iodine.

Example 8

In a glass lined mixing vessel, 1.7 ml of iodophor (Bardyne I-20 providing 20% titratable iodine, 2.5% (w/v)), is carefully blended by constant stirring into mixture of 10.0 ml of acetic acid and 10.0 ml of formic acid (88% assay) at 25°C. The resulting active agent intermediate is then stabilized and buffered by adding 9.0 ml of Product No. 92 buffering and stabilizing composition and blending slowly to homogeneity by constant stirring at 25°C. 70.3 ml of water is then added while stirring continues to obtain a buffered, stabilized homogenate. The resulting composition has an effective pH of between 3.8 and 4.0 and 2.0% available iodine.

Example 9

In a glass-lined mixing vessel, 0.83 ml of iodophor (Bardyne I-20 providing 20% titratable iodine, 1.25% (w.v)), comprising iodine and carrier, are

carefully blended by constant stirring into 20.0 ml of propionic acid and 20.0 ml of formic acid (88% assay) at 25°C. The resulting active agent intermediate is then mixed with 19.0 ml of Product No. 92 buffering and stabilizing composition and 42.17 ml of water.

Example 10

In a glass-lined mixing vessel, 0.83 ml of iodophor (Bardyne I-20, 1.25% (w.v)), comprising iodine and carrier, are carefully blended by constant stirring with 10.2 gm of lactic acid and 10 ml of formic acid (88% assay) at 25°C until dissolved. The resulting active agent intermediate is then mixed with 11.0 ml of Product No. 92 buffering and stabilizing composition and 69.17 ml of water.

Example 11

In a glass-lined mixing vessel, 0.83 ml of iodophor (Bardyne I-20, 1.25% (w.v)), comprising iodine and carrier, are carefully blended by constant stirring with 20 ml of propionic acid at 25°C. The resulting active agent intermediate is then mixed with 5.6 ml of Product No. 92 buffering and stabilizing composition and 73.57 ml of water.

Example 12

In a glass-line mixing vessel, 10.83 ml of iodophor complex containing 0.25% free iodine are carefully blended by constant stirring into 10.0 ml of acetic acid, 20.0 ml of propionic acid and 20.0 ml of lactic acid. The resulting active agent intermediate is then mixed with 5.0 ml of ammonia and _____ ml of water.

Example 13

In a glass-lined mixing vessel, 10.83 ml of iodophor complex containing 0.25% free iodine are carefully blended by constant stirring into 40.0 ml of propionic acid. The resulting active agent intermediate is then mixed to homogeneity with _____ grams of calcium hydroxide ($Ca(OH)_2$) and _____ ml of water.

Example 14

The antibacterial activity of the composition of the present invention prepared in accordance with Example 4 was compared with a number of biocide products presently available in the marketplace including Sal-Zap, Biosurf, Wescodyne and 1-Stroke Environ. Specifically, a gram negative bacterial culture was diluted to a final concentration of 2.5 - 3.0 x $10^6$ cells/ml and treated with the indicated biocide for an exposure time of 1 minute and 5 minutes. Treated cells were then transferred to recovery medium and allowed to incubate for the indicated time periods. Growth in the recovery medium was recorded as + (growth) or - (no growth). Table 1 indicating the results is set forth below.

Table 1

| Biocide | Exposure Time | Time After Transfer to Recovery Medium (hrs) 12 | 24 | 36 | 48 | 72 | 96 | 120 |
|---|---|---|---|---|---|---|---|---|
| Sal-Zap | 5 min | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
| | 1 min | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
| Biosurf | 5 min | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
| | 1 min | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
| Wescodyne | 5 min | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
| | 1 min | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
| 1-Stroke | 5 min | - | - | + | ++ | ++ | ++ | ++ |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1 min | - | + | ++ | ++ | ++ | ++ | ++ |
| Antimicrobial Composition of Example 4 | 5 min | - | - | - | - | - | - | - |
| | 1 min | - | - | - | - | - | - | - |

The above results are shown for bacteria exposed to the indicated biocide in the presence of 5% fetal calf serum. Clearly, the antimicrobial composition of the present invention displays significantly enhanced activity against gram negative bacteria over that displayed by commercially available products in an environment including organic matter (i.e. fetal calf serum and milk).

In a second comparative study, the treatment of biocide was carried out in the presence of 10% milk. The only observed difference in results as shown in the following Table 2 was that for 1-Stroke Environ.

Table 2

| Biocide | Exposure Time | Time After Transfer to Recovery Medium (hrs) 12 | 24 | 36 | 48 | 72 | 96 | 120 |
|---|---|---|---|---|---|---|---|---|
| 1-Stroke Environ | 5 min | + | ++ | ++ | ++ | ++ | ++ | ++ |
| | 1 min | + | ++ | ++ | ++ | ++ | ++ | ++ |
| Antimicrobial Composition of Example 4 | 5 min | - | - | - | - | - | - | - |
| | 1 min | - | - | - | - | - | - | - |

Example 15

The antibacterial activity of the composition of the present invention prepared in accordance with Example 4 was shown. Specifically, a broad spectrum of gram positive and gram negative bacteria was isolated from raw milk on blood agar. Cells from isolated colonies were then suspended in

either tap water plus 5% (v/v) fetal calf serum (FCS) or tap water plus 10% (v/v) milk (M) and treated with the present antimicrobial composition (1 to 100 dilution) for ten minutes at room temperature. 100 µl of treated cells were then transferred aseptically to 5 ml of a recovery medium (buffered peptone + M9 salts) and incubated at room temperature. The tubes were then examined for growth after 24 and 48 hours. At the end of the 48 hour incubation period, 50 µl of recovery medium from each treated culture was plated out on Luria-Bertani (LB) agar and examined for colonies after an additional incubation period at room temperature of 24 and 48 hours. Untreated cells were passed through the same steps (excluding treatment with the antimicrobial composition) to provide positive controls. Cells from the LB agar were gram stained and examined microscopically under oil immersion. The results are shown in Table 3 below ("-" indicates no growth; "+" indicates growth):

Table 3

| Bacteria | Incubation period | Growth after 10 minute treatment in 5% FCS | 10%M | Growth in LB agar |
|---|---|---|---|---|
| Encapsulated, beta-hemolytic Streptococcus | 24 hr | - | - | - |
| | 48 hr | - | - | - |
| Listeria sp. | 24 hr | - | - | - |
| | 48 hr | - | - | - |
| Non-hemolytic Streptococcus | 24 hr | - | - | - |
| | 48 hr | - | - | - |
| Unidentified Gram positive | 24 hr | - | - | - |
| | 48 hr | - | - | - |
| Unidentified | 24 hr | - | - | - |

| | | | | |
|---|---|---|---|---|
| Gram negative (pleomorphic) | 48 hr | - | - | - |
| Unidentified | 24 hr | - | - | - |
| Gram negative rod | 48 hr | - | - | - |
| Controls | 24 hr | + | + | + |
| | 48 hr | +++ | +++ | +++ |

Example 16

The antifungal activity of the composition of the present invention prepared in accordance with Example 4 was shown. Specifically strawberries on which Aspergillus sp. was growing were crushed and then incubated for several days until the strawberry juice was turbid. 5 ml of the turbid juice was then treated with a 1:256 dilution of the antimicrobial composition at room temperature for 30 minutes. Next the treated juice was diluted 1:50 with water and 1-2 ml of the diluted juice was mixed with a dried cornmeal and milk medium. The mixture was allowed to air-dry and then placed into a plastic bag and incubated at room temperature. 1-2 ml of untreated, diluted juice was also mixed with a sample of the dried corn meal and milk medium, air dried, placed into a separate plastic bag and incubated at room temperature (positive control). The results ("-" indicating no growth, "+" indicates growth) are presented in Table 4 below:

Table 4

| End-of-week | Growth of Aspergillus Treated Juice | Untreated Juice |
|---|---|---|
| 1 | - | + |
| 2 | - | ++ |
| 3 | - | +++ |
| 4 | + | ++++[a] |

[a] dried corn meal and milk medium completely covered by fungi

Example 17

Another comparative study was made to demonstrate the enhanced antimicrobial activity and beneficial synergistic effect of the composition of the present invention relative to the antimicrobial activity of iodine alone and various short chain fatty acid alone. Specifically, the procedure outlined in example 12 was followed with the following results:

Table 5

| Biocide | Exposure Time | Time After Transfer to Recovery Medium (hrs) 12 | 24 | 36 | 48 | 72 | 96 |
|---|---|---|---|---|---|---|---|
| Iodine 80 ppm | 5 min | ++ | ++ | ++ | ++ | ++ | ++ |
| | 1 min | ++ | ++ | ++ | ++ | ++ | ++ |
| Propionic Acid 0.04% | 5 min | ++ | ++ | ++ | ++ | ++ | ++ |
| | 1 min | ++ | ++ | ++ | ++ | ++ | ++ |
| Lactic Acid 0.0375% | 5 min | ++ | ++ | ++ | ++ | ++ | ++ |
| | 1 min | ++ | ++ | ++ | ++ | ++ | ++ |
| Propionic Acid (0.04%) and Lactic Acid (0.0375%) | 5 min | - | - | + | ++ | ++ | ++ |
| | 1 min | - | + | ++ | ++ | ++ | ++ |
| Antimicrobial Composition of Example 4 1:250 | 5 min | - | - | - | - | - | - |
| | 1 min | - | - | - | - | - | - |

Example 18

The corrosive activity of the composition of the present invention prepared in accordance with Example 4 was evaluated. Specifically, a 1:256 diluted solution of the composition was placed on samples of stainless steel and aluminum for a period of 24 and 36 hours. The solutions were then washed off and the metal was examined under magnification for indications of corrosion. No observable signs of corrosion of the metals were found when examined under magnification. Rubber O-rings were also allowed to soak in a 1:256 diluted solution of the composition for 24 hours and then examined under magnification. No observable cracking of the rubber when stretched or bent double were found when examined under magnification.

**********

In application, the composition of the present invention may be utilized as either a disinfectant on inanimate objects or an antiseptic on living tissue. Advantageously, the antimicrobial composition of the present invention approaches an ideal formulation as it has wide ranging activity against bacteria, fungi, viruses and protozoans under a wide range of environmental conditions. It is also buffered so as to be substantially non-corrosive and advantageously does not tend to stain or discolor materials on which it is utilized.

Accordingly, a method for disinfecting a surface of an inanimate object includes the step of applying to said surface an effective amount of an antimicrobial composition including one part 0.25-2.0% available iodine from an iodophor including a carrier acting as a solubilizing agent for said

iodine, 20.0 - 50.0% short chain fatty acid(s) selected from a group consisting of formic acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, isovaleric acid, lactic acid and mixtures thereof and 15.0 - 45.0% buffering agent and 50-800 parts water.

Similarly, a method for killing microorganisms on living tissue includes a step of applying to said living tissue an effective amount of an antimicrobial composition including one part 0.25 - 2.0% available iodine from an iodophor including a carrier acting as a solubilizing agent for said iodine, 20.0 - 50.0% short chain fatty acid(s) selected from a group consisting of formic acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, isovaleric acid, lactic acid and mixtures thereof and 15.0 - 45.0% buffering agent and 50-800 parts water.

Claims

1. An active agent intermediate for the preparation of a substantially noncorrosive antimicrobial composition, comprising by weight percent:

0.25 - 2.0% available iodine from an iodophor including a carrier acting as a solubilizing agent for said iodine; and 20.0 - 50.0% short chain fatty acid(s).

2. The active agent intermediate set forth in Claim 1 wherein said short chain fatty acid(s) is selected from a group consisting of formic acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, isovaleric acid, lactic acid and mixtures thereof.

3. The active agent intermediate set forth in Claim 2, wherein said carrier is a non-ionic surfactant and is provided at a level of between 6.0 and 25.0% by weight.

4. The active agent intermediate set forth in Claim 3, wherein said intermediate is diluted with between 50-800 parts water to one part iodophor and short chain fatty acid(s).

5. A substantially noncorrosive antimicrobial composition, comprising by weight percent:

0.25 - 2.0% available iodine from an iodophor including a carrier acting as a solubilizing agent for said iodine;

20.0 - 50.0% short chain fatty acid(s); and

15.0 - 45.0% buffering agent.

6. The antimicrobial composition set forth in Claim 5, wherein said short chain fatty acid(s) is selected from a group consisting of formic acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, isovaleric acid, lactic acid and mixtures thereof.

7. The antimicrobial composition set forth in Claim 6, wherein said buffering agent is selected from a group including known inorganic bases, organic bases, inorganic salts, organic salts and mixtures thereof.

8. The antimicrobial composition set forth in Claim 6, wherein said buffering agent is selected from a group including alanine, ammonia, ammonium acetate, ammonium benzoate, ammonium bicarbonate, ammonium hydroxide, benzoic acid, beryllium hydroxide, calcium acetate, calcium carbonate, calcium hydroxide, calcium tartrate, deuteroammonium hydroxide, diethylamine, glutamic acid, hydrazine, hydroxylamine, magnesium acetate, magnesium benzoate, manganese carbonate, manganese sulfate, potassium acetate, potassium bicarbonate, potassium carbonate, potassium citrate, potassium hydroxide, potassium phosphate, quinine, quinoline, sodium acetate, sodium ascorbate, sodium bicarbonate, sodium bisulfate, sodium carbonate, sodium citrate, sodium hydroxide, sodium phosphate, silver hydroxide and zinc hydroxide and mixtures thereof.

9. The antimicrobial composition set forth in Claim 7, wherein said composition is buffered to a pH between 3.5 and 4.5.

10. The antimicrobial composition set forth in Claim 9, wherein said carrier is a non-

ionic surfactant and is provided at a level of between 6.0 and 25.0% by weight.

11. The antimicrobial composition set forth in Claim 10, wherein said composition is diluted with water.

12. The antimicrobial composition set forth in Claim 10, wherein said composition is diluted with between 50 to 800 parts water to one part iodophor, short chain fatty acid(s) and buffer.

13. The antimicrobial composition set forth in Claim 5, wherein said buffering agent is selected from a group including known inorganic bases, organic bases, inorganic salts, organic salts and mixtures thereof.

14. The antimicrobial composition set forth in Claim 5, wherein said buffering agent is selected from a group including alanine, ammonia, ammonium acetate, ammonium benzoate, ammonium bicarbonate, ammonium hydroxide, benzoic acid, beryllium hydroxide, calcium acetate, calcium carbonate, calcium hydroxide, calcium tartrate, deuteroammonium hydroxide, diethylamine, glutamic acid, hydrazine, hydroxylamine, magnesium acetate, magnesium benzoate, manganese carbonate, manganese sulfate, potassium acetate, potassium bicarbonate, potassium carbonate, potassium citrate, potassium hydroxide, potassium phosphate, quinine, quinoline, sodium acetate, sodium ascorbate, sodium bicarbonate, sodium bisulfate, sodium carbonate, sodium citrate, sodium hydroxide, sodium phosphate, silver hydroxide and zinc hydroxide and mixtures thereof.

15. The antimicrobial composition set forth in Claim 5, wherein said composition is

buffered to a pH between 3.5 and 4.5.

16. The antimicrobial composition set forth in Claim 5, wherein said carrier is a non-ionic surfactant and is provided at a level of between 6.0 and 25.0% by weight.

17. A method for preparing an active agent intermediate for the preparation of a substantially noncorrosive antimicrobial composition, comprising:

mixing by weight percent substantially 0.25 to 2.0% available iodine from an iodophor including a carrier acting as a solubilizing agent for said iodine and 20.0 to 50.0% short chain fatty acid(s) selected from a group consisting of formic acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid and mixtures thereof.

18. A method for preparing a substantially noncorrosive antimicrobial composition, comprising:

mixing by weight percent substantially 0.25 to 2.0% available iodine from an iodophor including a carrier acting as a solubilizing agent for said iodine and 20.0 to 50.0% short chain fatty acid(s) selected from a group consisting of formic acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid, lactic acid and mixtures thereof; and

adding buffering agent.

19. The method set forth in Claim 18 wherein said buffering agent is selected from a group consisting of alanine, ammonia, ammonium acetate, ammonium benzoate, ammonium bicarbonate, ammonium hydroxide, benzoic acid, beryllium hydroxide, calcium acetate, calcium carbonate,

calcium hydroxide, calcium tartrate, deuteroammonium hydroxide, diethylamine, glutamic acid, hydrazine, hydroxylamine, magnesium acetate, magnesium benzoate, manganese carbonate, manganese sulfate, potassium acetate, potassium bicarbonate, potassium carbonate, potassium citrate, potassium hydroxide, potassium phosphate, quinine, quinoline, sodium acetate, sodium ascorbate, sodium bicarbonate, sodium bisulfate, sodium carbonate, sodium citrate, sodium hydroxide, sodium phosphate, silver hydroxide and zinc hydroxide and mixtures thereof.

20. The method set forth in Claim 19 including buffering said composition to a pH of between 3.5 and 4.5.

21. The method set forth in Claim 18, including diluting with water.

22. The method set forth in Claim 21, wherein said diluted composition includes between 50 to 800 parts water and one part iodophor, fatty acid(s) and buffering agent.

23. The method set forth in Claim 20, including diluting with water.

24. The method set forth in Claim 23, wherein said diluted composition includes between 50 to 800 parts water and one part iodophor, fatty acid(s) and buffering agent.

25. A method for disinfecting a surface of an inanimate object, comprising:

applying to said surface an effective amount of an antimicrobial composition including one part:0.25 - 2.0% available iodine from an iodophor including a carrier acting as a solubilizing agent for said iodine, 20.0 - 50.0% short chain fatty acid(s) selected from a group consisting of formic

acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, isovaleric acid, lactic acid and mixtures thereof and 15.0 - 45.0% buffering agent; and 50 to 800 parts water.

26. A method for killing microorganisms on living tissue, comprising applying to said living tissue an effective amount of an antimicrobial composition including 1 part:0.25 - 2.0% available iodine from an iodophor including a carrier acting as a solubilizing agent for said iodine, 20.0 - 50.0% short chain fatty acid(s) selected from a group consisting of formic acid, acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, isovaleric acid, lactic acid, and mixtures thereof and 15.0 - 45.0% buffering agent; and 50 to 800 parts water.

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 93/08967

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 A01N59/12 //(A01N59/12,37:36,37:02)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X | US,A,4 088 597 (G.MORLOCK) 9 May 1978<br><br>see column 2, line 23 - line 68<br>see column 3, line 28 - column 4, line 10<br>see column 4, line 44 - line 53<br>see the examples and claims<br>--- | 1,2,5-9,<br>13-15,<br>17-26 |
| X | DATABASE WPI<br>Week 8930, 1989<br>Derwent Publications Ltd., London, GB;<br>AN 89-217776/30<br>& JP,A,1 156 904 (SUNSTAR K.K.) 20 June 1989<br>see abstract<br>---<br>-/-- | 21-26 |

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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"P" document published prior to the international filing date but later than the priority date claimed

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"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 6 January 1994 | 20. 01. 94 |
| **Name and mailing address of the ISA**<br>European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax (+31-70) 340-3016 | **Authorized officer**<br>Muellners, W |

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# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 93/08967

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| A | SOAP AND CHEMICAL SPECIALTIES<br>vol. 33, no. 7 , July 1957 , NEW YORK, US;<br>PAGES 93, 95, 97, 105, 107<br>G.A BROST ET AL. 'Factors Influencing formulation and use of Iodophors as Sanitizing Agents'<br>see the whole document, in particular the chapter 'Formulations of Iodophors' | 1-26 |
| A | GB,A,950 954 (WEST LABORITORIES INC.) 4 March 1964<br>see page 1, line 12 - page 2, line 98<br>see page 5, line 23 - line 48 | 1-26 |
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| A | US,A,2 022 139 (G.MEDER) 26 December 1935<br>see page 1, line 1 - line 20 | 1-26 |

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information on patent family members

International application No.
PCT/US 93/08967

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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| GB-A-950954 | | NONE | |
| GB-A-272543 | | NONE | |
| US-A-2022139 | | NONE | |